Students in Politics

THE MOST TURBULENT academic year within memory is drawing to a close as this is written. One senses that faculty and students alike are exhausted, even limp, from the extreme emotional tensions of recent weeks. It is too early to assess what may have been achieved or what may have been destroyed. Curiously, perhaps inevitably, the exercise of bias and bigotry and even violence in protest against bias, bigotry and violence seems to have left less rather than more of these in its aftermath. Confrontations became convocations and teach-ins. The results were increased communication and understanding rather than the reverse.

There now appears to be developing a new attitude and a new approach for student action. At this writing it seems that the majority of students, rather than just the minority, have been aroused and seek involvement and action. This new majority has apparently concluded that external pressures of protest, confrontation and even violence have not been very effective in bringing about the changes which were sought and further they also seem increasingly sensitive to the illogicity of using violence to protest violence or repression. The result is a new attitude and a new approach although the goals of seeking change remain basically the same. There is now evident a growing commitment to work for the changes they want within the political system and through political action. This new approach has got under way with considerable ferver and speed under the impetus of the student reaction to Cambodia, Kent, Vietnam, and what they term the repressive racist policies of this nation at home and abroad. Political leaders at the local, state and national levels have felt its considerable impact.

This politicalization of student unrest, if it turns out to be something more than a flash in the pan, can signify a most constructive turn of events. It should mark the beginning of the end of a nightmarish era of too many "non-negotiable demands" of the few who by violence or threats of violence sought to impose their will upon all. It will permit the dialogue and free exchange of views necessary for a reasoned political concensus. This will encourage the involvement of all who should be involved if the political decision is to have the support of the majority and be carried to fruition. This is what our political system is all about, and if it has been lagging, or unresponsive, then student energy with expression of deep concerns should provide a potent stimulus. Everyone should benefit from this kind of constructive action by students in politics.

Viral Hepatitis: New Clinical, Epidemiological and Immunological Concepts

THE PAST TWO DECADES have been aptly called the "golden age of virology." The advent of tissue culture techniques has been followed by the isolation and identification of scores of viruses responsible for a variety of infectious diseases. In the wake of these advances came development of highly effective vaccines which have had a profound effect on the control of poliomyelitis, measles and other viral diseases. But despite intensive efforts by many investigators, the "golden age of virology" has been a barren and frustrating era for hepatitis research.

The discovery of Australia antigen by Blumberg and associates[1] represents a major breakthrough in hepatitis investigation. The association of this antigen with hepatitis has been highlighted in the proceedings of the UCLA Interdepartmental Conference devoted to "Current Concepts in Viral Hepatitis," printed elsewhere in these pages.

Recent studies by our group[2] have confirmed previous reports by Prince[3] and by Giles et al[4]

which established a definite association between Australia or hepatitis-associated antigen (HAA) and serum hepatitis (SH). Hepatitis-associated antigen was detected in 39 (97 percent) of 40 cases of SH; it was not detected in 41 consecutive cases of infectious hepatitis (IH). The discrepancy between these findings and reports by other investigators who have associated the antigen with IH is undoubtedly due to difficulties in clinical differentiation between IH and SH. Many physicians are not aware of the fact that both IH virus and SH virus can be transmitted by the oral and parenteral routes. It is still common practice to use the term SH for cases of post-transfusion or post-inoculation hepatitis and to reserve IH for situations where there is no history of a parenteral exposure.

Studies reported by our group in 1967[5] and in 1970[2] provided helpful clues for the clinical differentiation of the two types of viral hepatitis. Observations of patients who were observed from the time of exposure to IH or SH, during the incubation period and for many months after onset of disease, revealed the following: Infectious hepatitis was characterized by 1) a relatively short incubation period (30 to 38 days, average 33 days), 2) a brief period of abnormal transaminase activity (less than 3 weeks), and 3) consistently elevated thymol turbidity and IgM levels. In contrast, serum hepatitis was characterized by 1) a longer incubation period (41 to 108 days, average 65 days after parenteral exposure and 98 days after oral exposure); 2) a prolonged period of transaminase activity (35 to 200 days) and 3) normal thymol turbidity and IgM levels in most cases (approximately 75 percent). Studies of various epidemics during World War II indicated that the following additional clinical features were more compatible with SH than IH: Insidious onset, low-grade fever, urticarial rash and arthralgia.

At present the test for presence of HAA is the most helpful aid in differentiating between IH and SH. A positive test is indicative of serum hepatitis infection, past or present. A negative HAA test does not rule out SH because the duration of antigenemia may be transient; it may not be detectable shortly after onset of jaundice. Moreover, currently available immunodiffusion and complement fixation tests may not be sensitive enough to detect low levels of antigen.

The properties of the antigen have been described in detail by Gitnick elsewhere in this issue. It is clear that serum containing HAA is highly infectious for susceptible recipients. The transmission of serum hepatitis has been shown to be associated with the administration of serum containing virus-like particles 20 millimicrons in diameter. The circumstantial evidence indicates that the antigen is an intimate and integral part of serum hepatitis virus. If it is not the SH virus, it must be part of it or attached to it.

Each year, in the United States, blood transfusions are responsible for approximately 30,000 cases of hepatitis and about 3,000 deaths. It is well known that commercial donors are the major source of transfusion-induced hepatitis. At present the test for HAA holds the most promise as a hepatitis-screening procedure, in spite of the limitations alluded to previously—the lack of sensitivity of immunodiffusion and complement fixation techniques, and the inability to detect IH virus. In spite of these limitations, it will be essential for blood centers and hospitals to institute these procedures when appropriate reagents and technical manpower are available.

Our studies on the natural history of viral hepatitis have demonstrated that serum hepatitis virus is infective by mouth.[5] As indicated previously, the concept that serum hepatitis is exclusively a parenteral infection is not consistent with prevailing epidemiologic ideas about this disease. Patients on hemodialysis units and patients with blood dyscrasias who bleed profusely may be a source of SH virus dissemination if their blood is HAA-positive. Physicians, nurses and paramedical personnel who are exposed to these patients must take appropriate precautions to prevent infection which may be acquired by mouth or through a skin abrasion. It has been shown that 0.001 ml of infectious serum is capable of causing hepatitis in man.

The immunological aspects of viral hepatitis are poorly understood. It is likely that one attack of infectious hepatitis is followed by subsequent immunity to this disease. Evidence for homologous immunity has been well documented in the medical literature. It is clear, however, that an attack of IH does not protect against SH and an attack of SH does not protect against IH. Recent studies by our group revealed that an attack of serum hepatitis was followed by resistance to reinfection a year later.[2] These preliminary observations require additional confirmation.

Serum specimens from patients with serum hepatitis have been tested for the presence of anti-

body (anti-HAA). These tests have been consistently negative following the first or primary SH infection. On the other hand, antibody has been detected in some persons who have had repeated exposure to SH virus. Patients with hemophilia who have had multiple transfusions are apt to have detectable levels of anti-HAA in their blood.

The efficacy of gamma globulin for the prevention or modification of infectious hepatitis has been well documented. The same favorable effect has not been observed in persons exposed to serum hepatitis. Recent studies by our group demonstrated that gamma globulin neutralized the infectivity of IH virus but did not consistently neutralize the infectivity of SH virus.[2] These studies support the clinical impression that gamma globulin may have limited value for the prevention of serum hepatitis.

The treatment of viral hepatitis and hepatic coma has been discussed in detail elsewhere in this issue. The management of hepatic coma is still a critical problem. The role of exchange blood transfusions, isolated pig liver perfusion, and other new methods of therapy in the solution of this problem needs continuing study and evaluation.

It is obvious that the discovery of Australia or hepatitis-associated antigen has added a new and exciting chapter to the history of viral hepatitis. The availability of this new technologic tool has enabled many investigators to shed new light on the clinical, epidemiological and immunological aspects of viral hepatitis. However, as with poliomyelitis, measles and, more recently, rubella, the solution of the problem of control of hepatitis depends upon the isolation, identification and attenuation of the viruses responsible for hepatitis infection in man. It is hoped that the next chapter of the history of hepatitis will record this significant achievement.

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REFERENCES

1. Blumberg BS, Sutnick AI, London WT: Hepatitis and leukemia: Their relation to Australia antigen. Bull NY Acad Med 44:1566-1586, 1968

2. Krugman S, Giles JP: Viral hepatitis: New light on an old disease. JAMA 212:1019-1029, 1970

3. Prince AM: An antigen detected in the blood during the incubation period of serum hepatitis. Proc Nat Acad Sci USA 60:814-821, 1968

4. Giles JP, McCollum RW, Berndtson LW Jr, Klugman S: Relationship of Australia/SH antigen to the Willowbrook MS-2 strain. New Eng J Med 281:119-122, 1969

5. Krugman S, Giles JP, Hammond J: Infectious hepatitis: Evidence for two distinctive clinical, epidemiological and immunological types of infection. JAMA 200:365-373, 1967

Drug Eruptions

DRUG ERUPTIONS represent to physician and patient a troublesome by-product of pharmacologic therapeutics. To date its extent lacks precise fiducial enumeration because the prodigious time, energies and finances required to document the phenomena discourage the individual physician, the pharmaceutical industry and responsible governmental agencies.

In the Medical Progress article elsewhere in this issue, Newbold succinctly and clearly outlines the present status of our knowledge in this field. Diagnosis rests largely on a history of drug exposure (through one of many portals) and morphologic characteristics that may be almost diagnostic (phenolphthalien fixed drug eruptions or Sedormid purpura), suggestive (penicillin urticaria) or so highly atypical that a relationship is barely suspected. Unfortunately, many rashes of known and unknown type perfectly mimic drug eruptions, so our clinical diagnosis is probably often wrong.

This perilous dependence on clinical judgement in situations of serious consequences to the patient (that is, can he safely receive a needed drug?) prompted serious investigation of *in vivo* and *in vitro* diagnostic tests. Each advance in experimental immunology led to employment of the technique in drug eruptions. The roster includes skin tests for immediate and delayed hypersensitivity, quantitation of circulating humoral antibody, the basophile degranulation test, the Rebuck skin window technique and lymphocyte transformation studies. With few exceptions (such as Sedormid purpura) the highly variable results obtained emphasize our fragmentary understanding of the mechanisms involved. Even in penicillin hypersensitivity, where immense efforts have been expended to define the relationship of antibody to disease, the clinical situation remains unsettled. These techniques imply that antibody is probably involved in many drug eruptions. This may not be the case, as numerous examples of non-hypersensitivity eruptions have been delineated—for example, aspirin-induced histamine release and drug phototoxicity (see below).

As a practical issue, drug challenge constitutes the main diagnostic test to relate the suspected eruption to the drug. This is cumbersome for physician and patient; in some instances (such as peni-